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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s): Gleave, et al. Application No.: 10/646,391 Filed: 8/21/2003 Title: Treatment of Melanoma by Reduction in Clusterin Levels Attorney Docket No.: UBC.P-035 Customer No.: 021121	Group Art Unit: 1635 Examiner: Amy Hudson Bowman Confirmation No: 9734

Commissioner for Patents
PO Box 1450
Alexandria, VA 22313-1450

AMENDMENT

Dear Sir:

This is in response to the Office Action mailed September 7, 2005 for the above-captioned application. Reconsideration is respectfully requested.

The Examiner rejected claims 1-5 under 35 USC § 112, first paragraph, as lacking enablement. Applicants again traverse this rejection.

The Examiner asserts that the disclosure of activity of antisense sequences against clusterin in human melanoma cell lines *in vitro* and the general teaching as to the methods of employing this antisense in the treatment of melanoma is not sufficient to enable the methods of the invention. In support of this, the Examiner does not specifically state why undue experimentation would be required in the context of the present invention, but instead cites various references about general unpredictability associated with antisense technology. Applicants submit that this is insufficient.

I hereby certify that this paper and any attachments named herein are transmitted to the United States Patent and Trademark Office, Fax number: 571-273-8300 on October 26, 2005.

Marina T. Larson

Marina T. Larson, PTO Reg. No. 32,038

October 26, 2005
Date of Signature

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The challenges of using antisense as a therapeutic are fairly divided into two issues. The first is whether a particular nucleotide sequence will result in reduced expression when it is introduced into a cell. The second is whether this sequence can be delivered in vivo to the appropriate location to achieve the therapeutic goal. These are separate issues.

The Examiner again cites Branch, and states in that "Branch et al. is relied upon for the unpredictability of predicting RNA accessability *in vivo*, while the specification discloses *in vitro* testing." Applicants respectfully submits that the distinction between *in vivo* and *in vitro* testing that the Examiner is making in the context of the Branch reference is inaccurate. Branch teaches that not all antisense sequences will work because not all portions of the RNA are equally accessible to binding with the antisense. However, the accessability of RNA to antisense in an intact cell is no different whether that cell is in an *in vivo* or an *in vitro* environment because inside a living, intact cell, the RNA is in the same environment and is folded in the same way. Branch also teaches that there may be non-sequence-specific effects, and that these may be undesirable. Whether or not a given sequence will have side effects that make it a less-preferred pharmaceutical, however, is not relevant to the question of enablement. Here, Applicants have demonstrated the ability of multiple sequences to reduce the amount of clusterin expression in living cells. The Branch reference provides no basis to doubt that these sequences would have the same effect if delivered to a living cell in a living organism as opposed to in a living cell in a test tube. Thus, this aspect of the invention is fully enabled.

The evidence submitted in the declaration which the Examiner says is only convincing with respect to Seq. ID No. 4 relates to the issue. The declaration shows test results using clusterin antisense in connection with other clusterin-expressing tumors have shown that there are no special needs for delivery of the antisense. The Examiner has not offered any reasons that a person skilled in the art would believe that this result is sequence specific. Certainly, the generalized statement in the references cited are not sufficient to refute this evidence.

The Examiner rejected claims 1-5 under 35 USC § 102(e) as anticipated by Monia et al., US 2004/0053874); claims 1-5, 9 and 10 under 35 USC § 102(b) as anticipated by Gleave et al., WO 00/49937, and claims 1-5, 9 and 10 under 35 USC § 102(a) as anticipated by Gleave (US 2002/0128220). Each of theses reference disclose antisense therapeutic that target clusterin expression, but none of them mention their use in the treatment of melanoma.

In maintaining the rejection, the Examiner cites MPEP § 2112 for a teaching that "something that is old does not become patentable upon the discovery of a new property." Applicants point out, however, that all of the arguments recited by the examiner relate to composition/article claims, or to methods of making. The claims in the present application are not composition claims, nor method of making claims. The same section of the MPEP states that "the discovery of a new use for an old structure based on unknown properties of the structure

might be patentable to the discoverer as a process of using." *In re Hack*, 245 F.2d 246, 248, 114 USPQ 161, 163 (CCPA 1957). The Examiner has not addressed this issue in either this or the previous office action. Accordingly, if the Examiner is maintaining this rejection, it should be in a non-final action, since the Examiner's position is not properly in the record for purposes of appeal.

The claims of the present application recite "a method for treatment of melanoma in a mammalian subject." The Court of Appeals for the Federal Circuit has recently observed that

> In general, a preamble limits the [claimed] invention if it recites essential structure or steps, or if it is 'necessary to give life, meaning, and vitality' to the claim." *Catalina Mktg. Int'l, Inc. v. Coolsavings.com, Inc.*, 289 F.3d 801, 808, 62 USPQ2d 1781, 1784 (Fed. Cir. 2002) (quoting *Pitney Bowes, Inc. v. Hewlett-Packard Co.*, 182 F.3d 1298, 1305, 51 USPQ2d 1161, 1165 (Fed. Cir. 1999)). "[A] claim preamble has the import that the claim as a whole suggests for it. In other words, when the claim drafter chooses to use both the preamble and the body to define the subject matter of the claimed invention, the invention so defined, and not some other, is the one the patent protects." *Bell Communications Research, Inc. v. Vitalink Communications Corp.*, 55 F.3d 615, 620, 34 USPQ2d 1816, 1820 (Fed. Cir. 1995).

Eaton Corp. v. Rockwell International Corp., 66 USPQ2d 1271 (Fed. Cir. 2003). In the present case, the preamble cannot be deemed superfluous, since it says what is being accomplished by the method, namely a treatment of melanoma, and the claim without these words is meaningless. Indeed, the notion that preamble language is generally meaningless in method claims would render second use method claims impossible.

The importance of the preamble in method claims of this type is reflected in *Jansen v. Rexall Sundown, Inc*, 68 USPQ 2d 1154 (Fed. Cir. 2003). In that case, the claims at issue were directed to "a method of treating or preventing macrocytic-megaloblastic anemia" by administration of a composition of defined components "to a human in need thereof." The accused product was a dietary supplement having a composition as defined in the claims. It was labeled for uses that did not include treating or preventing macrocytic-megaloblastic anemia. The Federal Circuit found that the claims were limited to the use, as stated in the preamble. Similarly, in *Rapoport v. Dement*, 59 USPQ2d 1215 (Fed. Cir. 2001) a claims directed to "a method for treatment of sleep apneas" was interpreted as being just that, and not a method for treating symptoms associated with sleep apneas, which was found in the art.

In *Jansen* the Federal Circuit observed that

> in both *Rapoport* and this case, the claim preamble sets forth the objective of the method, and the body of the claim directs that the method be performed on someone 'in need.' In both cases, the claims' recitation of a patient or a human 'in need' gives life and meaning to the preambles' statement of purpose. The preamble is therefore not merely a statement of effect that may or may not be desired or appreciated. Rather, it is a statement of the intentional purpose for which the method is performed.

Jansen at 1158. In this case, the claim is directed to "a method for treating melanoma in a mammalian subject." Treatment is given to "the subject" and is "effective to reduce the effective amount of clusterin in the melanoma cells." Since there cannot be melanoma cells in a subject unless they have melanoma, this recitation is equivalent to the "in need" statements of *Jansen* and *Rapoport*. The rejection for anticipation should therefore be withdrawn.

The Examiner also maintained the rejection of claims 1-10 under 35 USC § 103 as obvious over the combination of Gleave (WO00/49937) in view of Barracchini (US 5,801,154). This rejection is dependent on the same assertions made in connection with the anticipation rejections and is in error for the same reasons. Baracchini does not disclose anything concerning melanoma or clusterin.

The Examiner also maintained the provisional obviousness-type double patenting rejection for the same reasons relating to statements of intended use. This rejection should be withdrawn for the same reasons as discussed above.

For the foregoing reasons, Applicants submit that this application is in form for allowance. Favorable reconsideration and allowance of all claims, including those withdrawn as a result of the restriction requirement are respectfully urged.

Respectfully submitted,

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